Report of the Board of Regents

Long Range Plan

National Library of Medicine

Improving Toxicology and Environmental Health Information Services



NATIONAL INSTITUTES OF HEALTH NATIONAL LIBRARY OF MEDICINE

National Library of Medicine Cataloging in Publication

National Library of Medicine (U.S.). Board of Regents

Improving toxicology and environmental health information services: report of the Board of Regents. — [Bethesda, Md.]: U.S. Dept. of Health and Human Services, Public Health Service, National Institutes of Health [1993]

"National Library of Medicine long range plan." "September 1993."

1. National Library of Medicine (U.S.). Toxicology Information Program. 2. Environmental Health 3. Information Services 4. Information Systems 5. Toxicology I. Title II. Title: National Library of Medicine long range plan

02NLM: Z 675.M4 N278ia 1993 Cit. No. 9305636 Report of the Board of Regents

Long Range Plan

National Library of Medicine

Improving Toxicology and Environmental Health Information Services

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Foreword

One of the lessons we seem destined to relearn again and again is that institutions, whether in the public or private sector, must successfully manage change. Unless there is a continuing commitment to renewal, organizations ossify and gradually become irrelevant in the contemporary world. Newspapers report almost daily about organizations that have failed to learn this simple lesson.

Through the adoption of a Long Range Plan in 1987*, the National Library of Medicine is meeting its commitment to managing change. The Plan is a living document that guides NLM decision-making. It wisely predicted that certain areas would need special attention in the future, and, under the direction of the Board of Regents, the Library subsequently brought together panels to look at outreach and medical imaging.

One of the goals for the Library identified in the 1987 Plan was to review its information services in certain public health areas, namely, those dealing with toxicology and environmental health. A Planning Panel was assembled and instructed by the Board to address these concerns. With this step, the Board initiated a planning process that moved forward with remarkable efficiency and ended with laudable results. The Panel was asked by the Board to address issues such as the near- and long-term needs of various user communities for informa-

tion about toxicology and environmental health: the commonalities and differences for such groups as health care providers, legislators, regulators, scientists, emergency response teams, and the public; the adequacy of existing information resources for present and foreseeable future information needs of these groups; the appropriate focus of NLM's efforts in this area; how NLM might improve access to its information services; and what new opportunities should be addressed by NLM (including opportunities stemming from new scientific discoveries, opportunities that are technology driven, opportunities resulting from the emergence of new classes of users, and opportunities that call for new collaborations with government agencies or other organizations).

The Board, on October 2, 1992, unanimously approved the report for incorporation in the Long Range Plan and applauded the leadership of its Co-Chairs, Edward N. Brandt, Jr., M.D., Ph.D., and Gilbert S. Omenn, M.D., Ph.D., and the hard work of all the members and the involved Library staff. Now begins the challenge—to assemble the resources and to implement the recommendations.

Lawrence Cohn, M.D. Chairman, Board of Regents National Library of Medicine

^{*}National Library of Medicine, Long range plan; report of the NLM Board of Regents. Bethesda, Md.: National Library of Medicine, January 1987.

Preface

The publication of Rachel Carson's *Silent Spring* in 1962 sounded a wake-up call to society, and worldwide concern about the deleterious effects of toxic agents on man and the environment has been increasing ever since.

Scientific inquiries into the nature and seriousness of these effects are growing, and governmental action, particularly in the United States and the other industrialized countries, to identify, prevent or at least alleviate such effects through laws, regulations, and public education are on the upswing. As with any area of science and technology, it is appropriate to examine the information base and the related information dissemination infrastructure that supports these inquiries and activities.

For the last twenty-five years, the National Library of Medicine, through its Toxicology Information Program, has been a leader in making information in toxicology and environmental health available to the professional communities that need it. While these subject areas and the related NLM activities were touched on briefly in the Library's 1987 Long Range Plan, there was not sufficient time then to examine them in detail and make recommendations for relevant NLM initiatives. It was, therefore, appropriate and timely for the Library's Board of Regents to ask that a Panel of Experts be assembled to reevaluate the goals, objectives, and scope of NLM's Toxicology Information Program considering current and likely future requirements for information and data in toxicology and environmental health, as well as likely advances for technology for information sciences.

The Panel's analyses, conclusions and recommendations are set forth in this report, which represents much serious discussion and diligent work on the part of the Panel members. We did not reach our conclusions lightly, and we did so in full recognition of the serious fiscal constraints faced by the Federal government. Nevertheless, it is our judgment that the provision of toxicology and environmental health information to a wide variety of users is a timely and important Federal investment. The members of the Panel gave generously of their time and talent, and we thank them on behalf of the Library. We are also grateful to Dr. Donald A.B. Lindberg, the Director of the National Library of Medicine, and to the capable NLM staff who assisted us throughout our deliberations; their good work made our tasks easier.

Edward N. Brandt, Jr., M.D., Ph.D. Gilbert S. Omenn, M.D., Ph.D. Co-Chairs, NLM Long Range Planning Panel on Toxicology and Environmental Health



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Executive Summary

In September 1990, the National Library of Medicine's Board of Regents recommended that as part of its continuing long range planning effort, the Library assemble a panel of experts to evaluate the goals, objectives, and scope of NLM's Toxicology Information Program, considering current and likely future requirements for information and data in toxicology and environmental health. A panel of distinguished experts in these areas was assembled and met three times in 1991 and 1992. The work of this panel culminated in this report to the Board of Regents.

The National Library of Medicine has operated a Toxicology Information Program (TIP) to create and provide information services in toxicology and environmental health for the last quarter century. A brief history of this Program is outlined in Appendix A. Although modest in resources, the TIP has been ambitious in scope and rich in accomplishments. In many cases these accomplishments have been directly attributable to a high degree of cooperation with other Federal agencies that brought with it not only expertise and guidance, but also the solution of joint problems and the provision of interagency resources to the Program.

The Panel was asked to review whether the needs of the users of toxicology and environmental health information services were being met and what changes might be needed to respond to changing circumstances and to take advantage of new opportunities. The ensuing report posits three broad goals and, under these goals, makes 16 specific recommendations.

GOAL 1: Provide Selected Core Information Resources and Services for Toxicology and Environmental Health

Recommendation 1.1. NLM should evaluate systematically the adequacy and extent of current library services in order to guide an expansion of its activities in collection building, cataloging, indexing, document delivery, and reference services in the subject areas of toxicology and environmental health. The Library should consider expansion of its MeSH indexing vocabulary and of the Unified Medical Language System (UMLS) project to accommodate these subjects. In addition, NLM should investigate the desirability of expanding its linkage to the several major libraries having substantial collections in these subject areas that are not now members of the National Network of Libraries of Medicine, offer to incorporate them into that network, and expand the network's interlibrary loan activities accordingly.

Recommendation 1.2. The NLM should extend its current outreach efforts to those working in toxicology and the environmental health sciences in an effort to ascertain from present and potential users the value of NLM's current database offerings and the need for additional database elements, components, or services. This effort should become part of a formal evaluation under which NLM periodically reassesses the contents and organization of its suite of toxicology and environmental health databases. NLM should evaluate the information needs of user

group categories that may not be well served by current offerings (e.g., practitioners of occupational and environmental medicine). A new user advisory group should provide advice on selection of databases for NLM's systems, and function as a forum for user feedback.

Recommendation 1.3. Based in part on the results of evaluation activities recommended in recommendation 1.2, NLM should develop a plan and a set of priorities for enhancing and expanding its information services to include additional data elements and, when expressly warranted, the offering of new factual, numeric, and geographic databases. A new user advisory group should provide advice on enhancing and refining NLM databases.

Recommendation 1.4. The contents of NLM's toxicological and environmental health databases should be integrated, where possible, so that they have common data elements, access methods, and indexing methodologies, and a consistent interface and uniform style. The objective is to allow these databases to be searched as a unit and ultimately linked with all MEDLARS databases.

Recommendation 1.5. NLM should include quality indicators and/or descriptors suitable for characterizing the sources of the contents of the databases available on its systems. This would include both databases produced by the NLM and, so far as possible, the offerings of other database producers distributing information via the NLM system. NLM should take a leadership role in encouraging other database producers to adopt quality indicators. Where such quality indicators do not

exist, NLM should attempt to establish indicators for NLM databases, and should make every effort to encourage adoption of successful indicators by other database producers.

GOAL 2: Facilitate Access to National and International Information Resources for Toxicology and Environmental Health

Recommendation 2.1. NLM should focus attention on the ease with which end users can access toxicological and environmental health information. New computer and information science technologies such as intelligent electronic gateway systems and artificial intelligence should be thoroughly evaluated and exploited, and combined with the results of studies of user needs to improve user access.

Recommendation 2.2. NLM should develop a directory of existing and accessible toxicological and environmental health information resources, using online computer and other distribution means. The directory should serve as a locator tool and an electronic linkage among the principal databases. It should facilitate users' access to databases that may not otherwise be easily available, especially non-NLM databases. Such a directory of information resources, while a large undertaking, should have as one goal to be an essential tool for risk assessment activities in Government and industry. This major task should be undertaken by NLM in concert with a new user advisory group.

Recommendation 2.3. As part of the High Performance Computing and Communications initiative, NLM should undertake further development of the Information Sources Map as a possible mechanism for implementing the directory for toxicology and environmental health information resources. Emphasis should be placed on databases supportive of health risk assessment activities.

Recommendation 2.4. Working with ATSDR, EPA, CDC, and other organizations with direct responsibility for emergency preparedness and response, NLM should continue its research to improve access to information helpful for these organizations and local agencies in managing emergencies such as chemical spills. Other information sources that are shown to be useful in emergency situations should be added to the ATSDR/NLM Workstation for Emergency Response (ANSWER) workstation.

Recommendation 2.5. NLM's current outreach efforts to improve access to toxicological and environmental health information by health professionals working with underserved populations should be strengthened. NLM should continue to place special emphasis on efforts directed to minority health education institutions and the communities they serve.

Recommendation 2.6. NLM should continue its historical emphasis on serving the information needs of professionals. While improved accessibility to NLM's databases should be established primarily for scientists and health officials, new access mechanisms for databases such as the Toxic Chemical Release Inventory (TRI) should be devel-

oped for the general public as well as professionals, and NLM should study the costs and benefits of such experiments.

Recommendation 2.7. NLM should systematically review international sources of relevant information and establish formal links with organizations whose databases would contribute to NLM's main goals in toxicology and environmental health. The review should pay special attention to the sources of information that may become available in Eastern Europe and Asia. NLM should collaborate with international programs in toxicology and environmental health such as those operated by the United Nations (UN) and its specialized agencies, the Organization for Economic Cooperation and Development (OECD), and the European Community, with the goal of facilitating access to these information resources by U.S. users. When resources permit, NLM should also offer technical assistance to countries endeavoring to improve their health and environmental databases.

GOAL 3: Strengthen the Information Infrastructure for Toxicology and Environmental Health

Recommendation 3.1. NLM should investigate possible new information structures and representations that are being used to aid in the understanding of the scientific basis of environmental effects on molecular and cellular systems. When there is sufficient accumulation of data, NLM should specify and design a prototype system for linking

chemical and toxicological data with a limited set of molecular databases, concentrating on toxic effects at the molecular and cellular level.

Recommendation 3.2. NLM should, expand its existing medical and biotechnology informatics research grants program to extend such research into areas that would advance the handling and use of toxicological and environmental health information, and in particular to facilitate research in the field of molecular toxicology.

Recommendation 3.3. NLM's authority should be amended to enunciate specifically the Library's continuing and

expanding responsibilities in the areas of toxicology and environmental health.

Recommendation 3.4. The National Academy of Sciences Toxicology Information Program Committee (TIPCOM) should be expanded in membership and scope of responsibility, and assume a more vigorous role in advising NLM in operational and technical matters, program policy, and new areas of science that should be addressed. A user advisory group comprised of representatives of NLM's enhanced user community should be organized under the auspices of TIPCOM to provide needed feedback on current and anticipated database offerings.



Charge to the Panel

In January 1985, NLM's Board of Regents undertook to develop a Long Range Plan to guide the Library in using its human, physical, and financial resources to fulfill its mission. Some 130 distinguished librarians, information scientists, physicians, nurses, biomedical researchers, computer scientists, and others took part. The Long Range Plan was adopted and published by the Board of Regents in 1987, and its recommendations are being implemented by NLM as resources permit.

The Board of Regents has since directed that the Plan be updated in selected areas, focusing on newly emerging areas and reconsidering some topics not completely specified in the original Plan. Two subsequent reports have been issued by the Board: Improving Health Professionals' Access to Information (the so-called "Outreach Report"), and Electronic Imaging. At its meeting in September 1990, the Board recommended that a planning effort for NLM's Toxicology Information Program be

instituted. Consequently a panel of experts was established.

The Panel was asked by the Board to address issues such as the near- and long-term needs of various user communities for information about toxicology and environmental health; the commonalities and differences for such groups as health care providers, legislators, regulators, scientists, and the public; the adequacy of existing information resources for present and foreseeable future information needs of these groups: the appropriate focus of NLM 's efforts in this area; how NLM might improve access to its information services; and what new opportunities should be addressed by NLM, including opportunities stemming from new scientific discoveries, opportunities that are technology driven, opportunities resulting from the emergence of new classes of users, and opportunities that call for new collaborations with government agencies or other organizations.

Goals and Recommendations

The history of life on earth has been a history of interaction between living things and their surroundings. To a large extent, the physical form and the habits of the earth's vegetation and its animal life have been molded by the environment. Considering the whole span of earthly time, the opposite effect, in which life actually modifies its surroundings, has been relatively slight. Only within the moment of time represented by the present century has one species—man acquired significant power to alter the nature of the world. 1 (Rachel Carson)

GOAL 1: Provide Selected Core Information Resources and Services for Toxicology and Environmental Health

The National Library of Medicine has been at the forefront of making toxicological and environmental health data accessible since the 1960's, when Rachel Carson's Silent Spring forcefully brought to the public's attention just how susceptible the environment was to widespread damage. NLM, through its Toxicology Information Program (TIP), has assembled highly useful databases that today are well-established mechanisms to search and retrieve needed information in such areas as toxicology, hazardous materials, occupational and environmental health, and the basic biomedical sciences. (A list of these resources is shown in Figure 1.) If the TIP is to continue to provide useful information resources it needs to undertake programs to strengthen

traditional library services, to evaluate the information needs of professionals working in toxicology and environmental health, to refine, expand, and integrate information in NLM databases, and to provide quality indicators for information sources.

1.1 Strengthen Traditional Library Services

The adequacy and extent of "traditional" library services in the areas of toxicology and environmental health, and the need for and use of these services, have never been fully evaluated. It is not known if existing library collections are sufficient. whether methods of bibliographic control—indexing and cataloging—are adequate, how well the established interlibrary loan processes serve the field, or whether existing reference services are satisfactory. For biomedical research and traditional clinical medicine, these functions are carried out within the 3.600-member National Network of Libraries of Medicine (NN/ LM). The Panel identified no equivalent systems serving toxicology and environmental health

How are the "traditional" library service needs of those working in the area of toxicology and environmental health now being met? What resources are available to meet these needs? How are they accessed? Would an employee of a state water pollution control agency know that the information she seeks is in the online Integrated Risk Information System (IRIS)? Or that the article she seeks can be quickly provided through the National Network of Libraries of Medicine? Any assessment of needs must take into



- TOXLINE (Toxicology Information Online): Toxicological, pharmacological, biochemical, and physiological effects of drugs and chemicals.

 Nonroyalty. 1.7 million records.
- TOXLIT (Toxicology Literature from special sources): Same as TOXLINE, but derived from royalty sources exclusively. 1.6 million records.
- CHEMLINE (Chemical Dictionary Online): Online dictionary of chemicals found in NLM databases and other sources. Royalty. 1.1 million records.
- *ChemID* (Chemical Identification): Online dictionary file of chemicals of regulatory and biomedical interest. Nonroyalty. 277,000 records.
- HSDB (Hazardous Substances Data Bank): Toxic effects, environmental fate, safety and handling data for hazardous chemicals. 4,300 records.
- CCRIS (Chemical Carcinogenesis Research Information System): Data on chemical carcinogens, mutagens, tumor promoters, and tumor inhibitors. 3,500 records.
- RTECS (Registry of Toxic Effects of Chemical Substances): Data on potentially toxic chemicals. 115,000 records.
- DBIR (Directory of Biotechnology Information Sources). 1,900 records.
- DART (Developmental and Reproductive Toxicology): Bibliographic information on physical agents that may cause birth defects. 12,000 records.
- EMICBACK (Environmental Mutagen Information Center Backfile): References to chemical, biological, and physical agents tested for genotoxic activity. 72,000 records.
- TRI (Toxic Chemical Release Inventory): Annual estimated releases of toxic chemicals to the environment and amounts transferred to waste sites. 335,000 records.
- IRIS (Integrated Risk Information): Contains chemical-specific EPA health risk data and regulatory information. 600 records.

Figure 1 NLM's Current Online Information Resources in Toxicology and Environmental Health



account the many types of individuals to be served, including physicians and nurses, HAZMAT personnel, emergency medical response teams, toxicologists, and environmental scientists.

Although NLM and the National Network of Libraries of Medicine do meet some of these information needs, the size of that portion is unknown. Moreover, although NLM does try to collect comprehensively published materials in toxicology and environmental health, the Library has never assessed its collection in these areas. The controlled vocabulary used to catalog and index these materials (Medical Subject Headings—MeSH), and the evolving Unified Medical Language

System (UMLS) have never been evaluated for their adequacy in these fields. Nor has there been any assessment of the collecting and archiving policies of the libraries in the NN/LM in this subject area, or of the borrowing patterns among them. In addition, some experts suggest that better bibliographic control of technical reports, state documents, and other elements of the "fugitive" literature is needed.

Recommendation 1.1

NLM should evaluate systematically the adequacy and extent of current library services in order to guide an expansion of its activities in collection building, cataloging, indexing, document delivery, and reference services in the subject areas of toxicology and environmental health. The Library should consider expansion of its MeSH indexing vocabulary and of the Unified Medical Language System (UMLS) project to accommodate these subjects. In addition, NLM should investigate the desirability of expanding its linkage to the several major libraries having substantial collections in these subject areas that are not now members of the National Network of Libraries of Medicine, offer to incorporate them into that network, and expand the network's interlibrary loan activities accordingly.

1.2 Evaluate the Needs of Users for Automated Information Services

In responding to the recommendations contained in Improving Health Professionals' Access to Information, the 1989 Planning Panel Report on Outreach, NLM has conducted a variety of successful outreach efforts to establish contact with potential users of its services. A similar effort is indicated to reach those working in toxicology and environmental health, such groups as HAZMAT personnel, emergency medical response teams. toxicologists, and environmental health scientists. Appropriate strategies for this include direct mail and online user surveys, focus groups, and outreach efforts (including exhibits at professional meetings) by the Regional Medical Libraries.

The purpose of reaching present and potential users is to learn on just which information services they place a high priority and where they feel the lack of adequate resources. Evaluating their needs might identify, for example, new elements to be included in NLM's present databases. Or perhaps a need will be expressed to add certain difficult-to-obtain databases to NLM's range of offerings, either by direct dissemination via NLM systems, distribution of databases or subsets to others, use of electronic gateways, or electronic directory listing.

Recommendation 1.2

The NLM should extend its current outreach efforts to those working in toxicology and the environmental health sciences in an effort to ascertain from present and potential

users the value of NLM's current database offerings and the need for additional database elements. components, or services. This effort should become part of a formal evaluation under which NLM periodically reassesses the contents and organization of its suite of toxicology and environmental health databases. NLM should evaluate the information needs of user group categories that may not be well served by current offerings (e.g., practitioners of occupational and environmental medicine). A new user advisory group should provide advice on selection of databases for NLM's systems, and function as a forum for user feedback.

The most difficult challenges for environmental health today come not from what is known about harmful effects of microbial agents; rather they come from what is not known about the toxic and ecological effects of the use of fossil fuels and synthetic chemicals in modern society. Population growth, urbanization, new energy sources, advanced technology, industrialization, and modern agricultural methods have enabled unprecedented progress. At the same time, they have created hazards to human health that are dramatically different from hazards of the past.2 (Healthy People 2000)



NLM should accelerate intramural R&D on products and services that are optimally responsive to the information needs of health professionals.³ (NLM Board of Regents "Outreach Report")

1.3 Refine and Expand Information Elements within NLM Databases

The suite of specialized databases in toxicology and environmental health that NLM now provides has been created de novo or acquired from diverse sources. The various databases contain many data elements, some unique, some in common. The evaluation to be undertaken in response to the previous recommendation may uncover inadequacies in these data elements, or may suggest linkages among them that do not presently exist.

The Panel identified a number of broad areas in which NLM should consider developing or enhancing databases. Examples are epidemiology, radiation, community emergency preparedness and response, and molecular medicine. Specific subject areas that appear to be inadequately covered are morbidity and mortality statistics related to environmental health. The user evaluation will no doubt suggest other areas-broad and specific—that require new or expanded information resources. In general, the Panel would expect to see the need expressed for more factual, numeric, and geographic data, in addition to bibliographic information.

Recommendation 1.3

Based in part on the results of evaluation activities recommended above, NLM should develop a plan and a set of priorities for enhancing and expanding its information services to include additional data elements and, when expressly warranted, the offering of new factual, numeric, and geographic databases.

A new user advisory group should provide advice on enhancing and refining NLM databases.

1.4 Integrate Information within NLM Databases

Because NLM's suite of toxicology and environmental health databases has evolved over the years in response to the needs of various agencies and organizations, there is little integration of the contents of the databases. They are built and maintained separately, and usually must be searched by the user one database at a time. In order to overcome this deficiency, however, NLM has begun to develop methods for crossfile searching of NLM databases. The Library should continue this effort, identifying common elements in toxicology and environmental health databases (even though they may derive from completely separate sources), and consider a system (such as a relational database structure) wherein the common elements are represented only once. File management would be more effective, data redundancy would be eliminated, and a variety of new service capabilities could be introduced.

Recommendation 1.4

The contents of NLM's toxicological and environmental health databases should be integrated, where possible, so that they have common data elements, access methods, and indexing methodologies, and a consistent interface and uniform style. The objective is to allow these databases to be searched as a unit and ultimately linked with all MEDLARS databases.

1.5 Label Computer Databases and Information Sources with Quality Indicators

Many of the current NLM databases in toxicology and environmental health take their content from datasets and other information collections that have been created by other organizations. Because of their various sources, such databases are lacking in consistent standards for scope of coverage, selection of individual entries, and contents. Data quality varies from database to database depending on the purposes for which the database was designed. Some databases are collections of carefully evaluated data; others may consist of estimated values. The same will be true for databases to which NLM users in the future might be directed through the electronic directory, pointers and linking systems.

NLM should not pass judgment on the validity of the data in a database, but for each should provide indicators of quality. For example, one indicator could specify that the database consists of raw experimental data obtained using Good Laboratory Practices. Another could inform the user that the data were extracted from peer-reviewed journals by a panel of experts. Other indicators could address breadth of subject coverage, completeness, relevance, and timeliness. Yet another could alert the user that the data were provided by the manufacturer of a particular chemical. and were not scientifically peerreviewed. Finally, data from some sources are not well characterized at all.

Recommendation 1.5

NLM should include quality indicators and /or descriptors suitable for characterizing the sources of the contents of the databases available on its systems. This would include both databases produced by the NLM and, so far as possible, the offerings of other database producers distributing information via the NLM system. NLM should take a leadership role in encouraging other database producers to adopt quality indicators. Where such quality indicators do not exist, NLM should attempt to establish indicators for NLM databases, and should make every effort to encourage adoption of successful indicators by other database producers.



GOAL 2: Facilitate Access to National and International Information Resources for Toxicology and Environmental Health

An important long-term goal for NLM has always been to facilitate access to toxicology and environmental health data and information that may not otherwise be easily available. To do this, NLM identifies such resources and makes them accessible either by linking them into networks, describing them in directories, or by establishing cooperative arrangements between NLM and providers of information. Perhaps in the future potential users may see an electronic composite or "seamless" system in which "intelligent" system agents guide the user query throughout all relevant parts of the composite network of linked (and mutually referential) knowledge sources.



The image represents the interconnected "backbone" networks of NSF, NASA, and DOE, together with selected client regional and campus-area networks. Nodes of the backbones are represented as connected spheres on a plane above the outline of the United States; the client networks are represented as dendritic lines from the backbone nodes to the geographic locations where the client networks attach.

2.1 Continue to Improve Access to Information Products and Services

For the MEDLARS files, NLM can point to great success with user-oriented information products and services, such as Grateful Med, the personal-computerbased front end searching package, and the recent development of Coach, an expert searcher system. Coach brings to bear the UMLS Metathesaurus and other knowledge sources to assist Grateful Med users seeking help in improving retrieval from MEDLARS. These interface programs have been shown to satisfy the needs of health professionals and also have been effective in outreach efforts focused on health professionals serving minority, rural, and other underserved populations. There is a need for similar advances for the toxicology and environmental health information resources.

Recommendation 2.1

NLM should focus attention on the ease with which end users can access toxicological and environmental health information. New computer and information science technologies such as intelligent electronic gateway systems and artificial intelligence should be thoroughly evaluated and exploited, and combined with the results of studies of user needs to improve user access.

2.2 Develop a Directory for Toxicology and Environmental Health Information Resources

Many of the databases in toxicology and environmental health are not NLM databases now, nor-for various reasons—are they likely to become part of the NLM dissemination systems in the future. Few of these databases were designed to serve a broad spectrum of users. Most were developed by individual organizations to meet their specific information needs. It is difficult for the user to identify appropriate databases to search for answers to specific questions and to learn how to extract information from those databases once identified. Some databases (such as files that contain confidential business information) are restricted in their use; others require significant training.

NLM could make an important contribution by developing, maintaining, and promoting a directory of databases in toxicology and environmental health i.e., a system with "pointers" to available public and private resources. A properly designed directory would go a long way toward facilitating the use of toxicology and environmental health information by answering questions about where information can be found and how it can be accessed. Such a directory of databases could contain indications of the content of the database, characterizations of the data quality, and instructions on how to use the database. The directory is itself a database, and there are many possible formats for its delivery to users—electronic online access, CD-ROM, printed, and perhaps future forms such as computer knowledge sources, imbedded within software intelligent agents.

The Panel is aware of the current study being sponsored by the Federal Coordinating Council for Science Engineering and Technology (FCCSET) concerning the feasibility of building a comprehensive directory of databases that could be used as information resources for health and ecological risk assessment activities.5 Health risk assessment—the use of available information to evaluate and estimate exposure to a hazardous agent and its consequent adverse health effects—depends on the availability of accurate, up-to-date scientific information. Because risk assessment plays a significant role in Government regulatory priority setting and decision making, improving the process will provide better support for setting priorities both in the control of existing risks and in the development of new technologies with reduced risks.

A computer-based directory would permit the development of a number of access tools that would employ informatics, expert systems, and gateway technologies to reach and search selected databases. An expert system based on the data in the directory could be developed to help the noninitiated user find the pertinent sources to meet specific information needs. NLM research efforts in informatics could be brought to bear on this aspect of the directory. Another option would be a gateway network system that not only would tell the user where information could be found, but—when technically feasible—would connect the user directly to the systems to be accessed. If the target databases are not available online, the access system could help to generate a request to obtain the information.

Legislators and policy makers need better information to make good laws and regulations; public health officials need better information to detect and prevent the health effects of exposure; and the public deserves information that is understandable...⁴ (National Research Council)

The marshaling of resources, public and private, to insure better health for the American people has been a phenomenon of the post-World War II decades.... Attention has been called repeatedly to a significant exception to this commendable development. Those problems which are associated with the communication of new scientific knowledge, both to researchers who must use it still further to explore the unknown, and to practitioners who must have access to it to improve the Nation's health, are so critical as to warrant our most serious attention.6 (President's Commission on Heart, Cancer and Stroke)

Ultimately, such an electronic directory database could provide the foundation for a system that would integrate databases using distributed network technology to bring to the user the actual desired information, rather than just pointing to where it could be obtained.

Recommendation 2.2

NLM should develop a directory of existing and accessible toxicological and environmental health information resources, using online computer and other distribution means. The directory should serve as a locator tool and an electronic linkage among the principal databases. It should facilitate users' access to databases that may not otherwise be easily available, especially non-NLM databases. Such a directory of information resources, while a large undertaking, should have as one goal to be an essential tool for risk assessment activities in Government and industry. This major task should be undertaken by NLM in concert with a new user advisory group. An NLM effort in this area should be coordinated with other similar Federal efforts.

2.3 Develop the Information Sources Map as a Way to Implement the Directory for Toxicology and Environmental Health Information Resources

The Information Sources Map (ISM) component of NLM's Unified Medical

Language System is being developed as part of the Library's contribution to research in the national High Performance Computing and Communications project. The ISM appears to embody the functional goals of the toxicology directory; it provides both human and machine readable descriptive information on the content and access conditions for computerized information sources, and the ability to select information sources automatically based on the subject and type of information sought. The goal is to allow users to state simply what information is sought, to have the ISM determine likely sources for that information, and to retrieve it in a manner that does not require a user to learn the syntax or inner structure of the system being queried.

Prototype efforts to expand the number of information sources represented in the ISM currently include some that are relevant to toxicology and environmental health. Depending upon the financial resources that can be assigned to this activity, particular emphasis should be placed on databases supportive of health risk assessment activities.

Recommendation 2.3

As part of the High Performance Computing and Communications initiative, NLM should undertake further development of the Information Sources Map as a possible mechanism for implementing the directory for toxicology and environmental health information resources. Emphasis should be placed on databases supportive of health risk assessment activities.

2.4 Support Information Access for Emergency Preparedness and Response Programs

NLM's mandate to provide information support for health care includes the health-related aspects of emergencies. The ever-increasing likelihood of emergencies involving hazardous chemicals is forcing both the emergency management community and the health professions to reexamine how they can prevent, mitigate, or respond to such emergencies. One such incident is described in Figure 3.

NLM's TIP, with the Agency for Toxic Substances and Disease Registry (ATSDR), has built a portable, microcomputer-based workstation that provides information assistance to emergency response teams working on accidents involving hazardous chemicals. The prototype, known as ANSWER (an acronym for ATSDR/NLM's Workstation for Emergency Response), consists of software modules designed to facilitate easy access to information useful to response teams during emergencies. A graphic representation of the workstation is shown in Figure 2.

In 1991, the Workstation was made available for beta testing at 13 sites, including selected state health departments and several poison control centers. The results of the test show that ANSWER is fully functional in a command center environment in both emergency and nonemergency situations. Further, the test shows that chemical databases on CD-ROM in addition to the Hazardous Substances Data Base (HSDB) would be very helpful in the field.

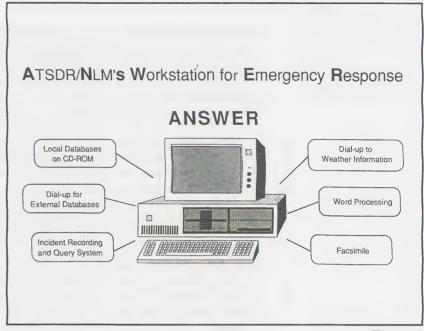


Figure 2



Emergency Response: A Quiet July Afternoon ⁷

DESCRIPTION: The time is **2:07 P.M.** on the afternoon of July 18, 1985. It is a typical July afternoon in the Ohio River Valley. The temperature is in the high 80's, low 90's; the humidity is high and there is little if any air movement. The threat of an afternoon thunderstorm is present. Suddenly, the quiet of the afternoon is shattered by an explosion at a chemical manufacturing plant in southwest Jefferson County, Kentucky. A giant fireball erupts. Two welders who were on top of the tank are killed immediately; a third is thrown clear of the tank but suffers third degree burns over eighty percent of his body. An emergency call is placed to 911; the call is routed to the fire alarm office. Fire alarm personnel notify the volunteer fire protection district and activate the local hazardous material response team. Notification is then given to state response agencies.

THE FIRST AFTERNOON: 2:15P.M.: First on scene fire units are confronted with a fireball approximately 40 feet in height. Having been on the scene before, fire personnel recognize the fireball to be in the tank farm area of the facility. Located here are some 20 to 30 storage tanks averaging approximately 12,000 gallons capacity each. Plant personnel are not able to immediately advise as to the cause of the explosion or the materials involved. The principle product at this facility is a phenol-formaldehyde based resin. Upon entry to the explosion area, firefighters find a 16 foot high, 10 foot diameter tank which has been blown off its foundation. The liquid from within the tank is now burning within the diked area of the tank farm and impinging on other tanks. Plant personnel have started a water stream to cool other tanks and reduce the likelihood of further explosions. Fire personnel immediately begin to add additional cooling streams. The injured employee is taken by air ambulance to the trauma/adult burn center in downtown Louisville.

2:30P.M.: Hazardous material response units from the Health Department and other agencies begin to arrive. Facility personnel advised that the material is a phenolformaldehyde resin in a methanol solvent. Surrounding tanks contain phenol, formaldehyde and methanol. The plant safety engineer advises that the by-products from the fire are unknown and could be hazardous. The plant manager advises that the materials are non-hazardous and that no special precautions need be taken. Haz-Mat personnel begin to research the product information in both written references and by computer hook-up to remote databases. Specific concerns include:

- Safety / protection of fire personnel involved in firefighting effort
- Protective actions necessary for citizens downwind from event
- Treatment necessary for injured and contaminated worker
- Control of potential contamination spread to air ambulance and hospital
- Identification of special land uses downwind (i.e.: schools, nursing homes)

Information needs identified include:

- Physical, chemical and health hazards of non-combusted materials and of combustion by-products
- Meteorological information
- Land uses and populations within a one mile radius
- Inventory of all plant materials

2:40P.M.: Precautionary evacuation of surrounding area (approximately 150 persons) is begun by law enforcement personnel. Firefighting and tank cooling efforts continue. Additional response units from state and local agencies continue to arrive. Data hook-ups are established to access remote hazardous material databases. An on-site meteorology station is erected. Information collected is used to predict possible path of the plume.

3:30P.M.: The fire has been put out but cooling streams continue. Firefighters begin to complain of headaches and other physical problems that could be related to either product exposure or heat stress. Local elected officials arrive at the scene to assess damage and are taken on a tour by the plant manager. Information received from databases, etc. is sent to hospital and shared with regional poison control center. No information on product mixture or combustion by-products can be found (a MSDS is available but lacks any specific treatment information beyond the first aid level).

5:00P.M.: Decision is made to lift the evacuation request and allow persons to return to their homes. Shortly after decision is made, another fire breaks out in general area of tanks. Decision is rescinded and evacuation put back into place.

6:00P.M.: Second fire is put out and evacuation is lifted.

10:00P.M.: Fire department representatives contact the health department regarding decontamination/disposal of contaminated fire gear that was taken from the scene. Fire service advised to bag materials and await outcome of next day investigation.

THE SECOND DAY: Residents upwind from the site but impacted by the blast and the evacuation begin to ask questions regarding fitness for consumption of products grown in their gardens. Residents are advised that based on the information available, fruits and vegetables that can be washed should be OK. Industry representative requests that all response personnel, including local elected officials, report to local hospital for "blood tests". This raises significant questions among responders as to the actual potential for long term health effects. Fire, police, some emergency medical service personnel and local elected official go to hospital for "blood test". Director of health asked to explain why this is necessary and what is expected outcome. Industry representatives request that all potentially contaminated clothing and equipment be bagged and returned to the plant for decontamination and or disposal. Third worker who was injured in original explosion and fire dies.

TWO WEEKS LATER: Citizens still expressing concerns about crops. Some plants are turning brown and dying. The county agricultural agent is requested to survey the area. He does so but is not able to make a definitive statement as to cause of plants dying. State special agent for plant pathology is brought in to survey area in question. All problems can be explained by normal insect, plant disease and ozone damage (Jefferson County had been under an ozone warning approximately two weeks before the explosion).

Figure 3.
Planning Panel on
Toxicology and
Environmental
Health,
March 24, 1992,
Clark Bledsoe

Other information resources for emergency preparedness and response are available, including Materials Safety Data Sheets, TOMES, EIS, and CAMEO (see glossary). These systems contain information about such areas as facility site plans, maps and geographic data, health care facilities, plume dispersion models, chemical inventories, and medical management of chemical exposures, and have the capacity for presenting dynamic, electronic map overlays.

Recommendation 2.4

Working with ATSDR, EPA, CDC, and other organizations with direct responsibility for emergency preparedness and response, NLM should continue its research to improve access to information helpful for these organizations and local agencies in managing emergencies such as chemical spills. Other information sources that are shown to be useful in emergency situations should be added to ANSWER.

2.5 Support Information Access by Professionals Serving Underserved Populations

NLM has placed a high priority on outreach to health professionals in underserved communities, specifically with the purpose of improving access to NLM information services. Environmental issues are of concern to underserved populations, including racial minorities and the socioeconomically disadvantaged, who tend to be disproportionately exposed to hazardous environmental conditions at home and in the workplace.⁸

NLM has under way a program to enhance the capability of students and faculty at Historically Black Colleges and Universities (HBCUs) to use the toxicological, environmental, occupational, and hazardous waste information resources available from the NLM. HBCUs are the training ground for many of the health professionals who will ultimately practice in underserved communities. These institutions are also uniquely positioned to channel needed information to neighboring communities possibly affected by exposures to toxic chemicals and other hazardous materials. This information can be vital for purposes of prevention. diagnosis, treatment, and public awareness.

Recommendation 2.5

NLM's current outreach efforts to improve access to toxicological and environmental health information by health professionals working with underserved populations should be strengthened. NLM should continue to place special emphasis on efforts directed to minority health education institutions and the communities they serve.

2.6 Emphasize Service to Health Professionals

NLM has a long-standing policy of focusing its products and services on the needs of health professionals rather than the general public. A primary reason for this is the near-impossibility of acquiring, organizing, and making accessible the huge volume of publications prepared for use by the lay public with the resources even remotely foreseen for the Library. The NLM Board of Regents has stated, "While the distinction between health education for the public and education for the health professional is not absolutely clear, the prime responsibility of the NLM is the organization and dissemination of knowledge which has applicability to the needs of health professionals. The statutory responsibility for health education for the public resides in other Federal agencies."9

In its 1987 Long Range Plan¹⁰, the Board re-examined this issue and recommended that NLM study current sources of health information for the public and the potential role for NLM in this area. It also recommended that NLM augment DIRLINE-an NLM online directory of information-providing organizations—to provide a more complete directory of sources of health information for the lay public. NLM has expanded DIRLINE coverage as recommended. Regrettably, this task has become more difficult for NLM, since the Library of Congress stopped maintaining the National Referral Center database, which had constituted the core of DIRLINE. Because of the daunting investment that would be needed to collect and organize the huge body of



published health information for the public, NLM has not initiated efforts in this area beyond expanding DIRLINE.

The Toxic Chemical Release Inventory (TRI) presents a special case. TRI, which contains data on the releases of over 300 toxic chemicals into the air, water, and land, is used largely by emergency personnel and environmental organizations. The Environmental Protection Agency, however, is required to provide the TRI data to the general population and has entered into an interagency agreement with NLM to make the data available through TOXNET. NLM is working to provide a clear and easy-to-use interface to TRI for lay and professional users.

From the Baltic to the Black Sea, half a century of runaway industrialization has left a smear of destruction through the heart of Eastern Europe.¹¹ (National Geographic)

Recommendation 2.6

NLM should continue its historical emphasis on serving the information needs of professionals. While improved accessibility to NLM's databases should be established primarily for scientists and health officials, new access mechanisms for databases such as the Toxic Chemical Release Inventory (TRI) should be developed for the general public as well as professionals, and NLM should study the costs and benefits of such experiments.

2.7 Enhance Access to International Information Resources

A significant amount of the healthrelated information collected and disseminated by NLM comes from abroad. In 1879, when the Library published the first issue of *Index Medicus* (IM), 530 of

the 660 journals indexed in *IM* (80%) were from outside the U.S. Today, a significant amount of the information collected by NLM continues to come from non-U.S. sources—the comparable non-U.S. *IM* figure today is 63%—and much of the literature cited from U.S. sources derives from the work of international researchers.

Concerns about the environmental effects on human health are global, and not confined to the U.S. Chemicals are produced, traded, and used throughout the world in increasingly large numbers and quantities. Once released into the environment, they may be transported deliberately or inadvertently across wide distances by air or water or in food. They may be accumulated or transformed in plants, animals, and humans. Thus, environmental chemicals pay no attention to national boundaries. Some, such as those causing atmospheric changes, may affect human health globally in different ways and to different degrees in many countries for many years. In addition to global phenomena, each country or region will have data on the effects that are most prominent there.

NLM is in a position to offer substantial technical assistance to countries endeavoring to improve their health and environmental databases. In its ongoing international program, the Library now provides technical support to some countries seeking to develop regional or national biomedical information systems. If resources permit, NLM should consider taking a more systematic and active role in providing both information and technical assistance to more countries.

Obviously, information from around the world is important to reducing health risks to American citizens resulting from contamination of the environment. The need for international data sharing has never been more important. The globalization of the economy and of science and technology is bringing into sharper relief the importance of international data in toxicology and environmental health for U.S. research and development, academic instruction and curriculum development, and development of the scientific foundations for public health policy and health services.

There is intensified research in this area, particularly in industrialized countries. In addition, many governments have adopted laws controlling chemical risks. These laws for the testing and risk assessment of chemical substances and industrial facilities are often similar to U.S. laws, and are providing a basis for many specialized databases. International and regional efforts in these areas that should be considered for collaboration with NLM are the United Nations Environmental Programme (UNEP) International Register of Potentially Toxic Chemicals (IRPTC), the joint ILO/UNEP/WHO International Programme on Chemical Safety (IPCS), OECD's Chemicals Programme, and relevant activities of the European Community (EC).

NLM cannot afford to ignore the intellectual, informational, or financial resources represented by these activities in other countries. It is important to have access to these databases to avoid costly and unnecessary duplication of effort, and to allow health professionals and researchers in the United States to benefit from the worldwide growth in understanding about toxicology and environmental health problems.

Recommendation 2.7

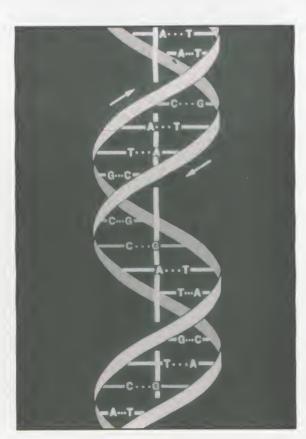
NLM should systematically review international sources of relevant information and establish formal links with organizations whose databases would contribute to NLM's main goals in toxicology and environmental health. The review should pay special attention to the sources of information that may become available in Eastern Europe and Asia. NLM should collaborate with international programs in toxicology and environmental health such as those operated by the UN and its specialized agencies, the OECD, and the European Community, with the goal of facilitating access to these information resources by U.S. users. When resources permit, NLM should also offer technical assistance to countries endeavoring to improve their health and environmental databases.

To advance a society's health goal ... depends on optimizing the environmental determinants of health...The quality of decisions ... depends on the proper communication of accurate information to decision-makers. public and private, entrepreneurial and domestic. 12 (World Health Organization)

For mankind as a whole, a possession infinitely more valuable than individual life is our genetic heritage, our link with past and future. Shaped through long eons of evolution, our genes not only make us what we are, but hold in their minute beings the future—be it one of promise or threat. Yet genetic deterioration through man-made agents is the menace of our time, "the last and greatest danger to our civilization." 13 (Rachel Carson)

GOAL 3: Strengthen the Information Infrastructure for Toxicology and Environmental Health

In order for NLM to accomplish the mission set forth in the previous two goals, it is important that certain organizational ("infrastructure") issues be clarified. These involve the importance of NLM positioning itself vis-a-vis future scientific discovery in toxicology and environmental health, the value of providing support to informatics researchers nationwide in these fields, the need to obtain a broader spectrum of advice for NLM information services in toxicology and environmental health, and the advisability of requesting clarification of certain legislative authorities.



3.1 Provide an Information Infrastructure for Future Scientific Discovery in Toxicology and Environmental Health

Future progress in the disciplines that support research and development in toxicology and environmental health is dependent on information resources adequate to their needs. The use of NLM's online services in emergency situations and at the community level is one end of the continuum; at the other is the need of scientists who generate new data and who depend on an ever richer and more sophisticated information environment to support their work. If these are to be mutually reinforcing, the NLM must constantly be alert to sources of new data and to new ways of linking existing data to ensure that what we learn about the environment broadly is turned to maximum use for society.

The Panel believes that a key part of this long-term goal is the development of integrated databases and data handling capabilities that will identify and link the toxic effects of chemical agents to their molecular structures and to the cellular sites of toxic actions.

A recent FCCSET Committee report states that "Biotechnology is a set of powerful tools based on biological knowledge. Mastery of these tools will ultimately touch every facet of American life from the food we eat and the water we drink to the energy that fuels our machines and the materials from which they are constructed. Biotechnology offers novel approaches to conquering disease, easing world hunger, and reducing environmental pollution...The impact

of biotechnology on society and the economy in the coming decade could be profound, and grow dramatically in the next century, if projected technical advances are realized."14

The rapidly growing body of knowledge about the molecular basis of life is taking the form of computer-based factual databases with explicit links to bibliographic records of the published scientific literature, and implicit links to other factual databases. An example is the GenBank record of nucleic acid sequences of genes (or gene fragments), its links to MEDLINE records of the peer-reviewed publications announcing the discoveries, and its merely implicit links to the records of the amino acid sequences that characterize the protein products of the same gene (see Figure 4).

In addition to such relatively well-known examples, scientists are also reporting the occurrences of molecular changes that may be important "biological markers" for the permanent effects of environmental hazards upon a susceptible population (or individual). By and large, the current design of computer databases does not yet reflect such relationships. NLM should monitor the field and take action so that important scientific data and associations are not obscured within the growing mass of facts.

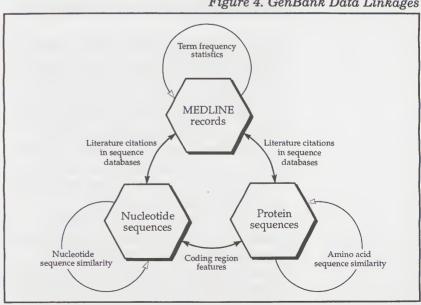
As more knowledge about the molecular basis of life becomes available, it is important that the molecular and cellular basis of toxicological effects be considered as an organizing principle for future databases. As a starting point, NLM should undertake to analyze current chemical and toxicological databases with a view to establishing linkages between those and other databases that deal with molecular information. such as genetics, mapping, and sequence databases.

Recommendation 3.1

NLM should investigate possible new information structures and representations that are being used to aid in the understanding of the scientific basis of environmental effects on molecular and cellular systems. When there is sufficient accumulation of data, NLM should specify and design a prototype system for linking chemical and toxicological data with a limited set of molecular databases, concentrating on toxic effects at the molecular and cellular level.

We are on the leading edge of a great wave of research, research that will produce better data and better models, research that will provide regulators with the tools to reduce exposure and protect the public health. There's at least a B-1 bomber's worth of research needs... 15 (National Research Council)

Figure 4. GenBank Data Linkages



3.2 Initiate Support for Extramural Research in Toxicological and Environmental Health Informatics

With funding and leadership provided by NIH and NLM, a community of researchers has been active for over two decades in wide-ranging applications of computers to medicine. This research has greatly advanced the capabilities of the computer in research and medical decision making and has laid the groundwork for substantial work yet to be done. Specifically, medical informatics research support has resulted in new information management tools, methods for representing the judgment and knowledge of experienced physicians, computer networks to permit efficient communication among health personnel, and expert computer systems to provide advice and decision support to health workers and to monitor health care. The value of such tools will be enhanced progressively as increasingly powerful computer systems and user-friendly interfaces are developed.

There is a need to extend these informatics technologies to areas pertinent to toxicology and environmental health, such as epidemiology, pharmacokinetics, risk assessment, toxic plume dispersion, disaster modeling, and chaos theory. Application of modern informatics technologies is particularly important for new subfields like "molecular toxicology" and "molecular epidemiology." Similarly, there is a need to support research to address pressing needs in the organization and representation of knowledge about toxicology and environmental health. A desirable mechanism to support such research is by extending current NLM grant programs.

Recommendation 3.2

NLM should expand its existing medical and biotechnology informatics research grants program to extend such research into areas that would advance the handling and use of toxicological and environmental health information, and in particular to facilitate research in the field of molecular toxicology.

3.3 Define NLM Responsibilities in Toxicology and Environmental Health

TIP has implemented its products and services in response to major environmental laws that mandate other agencies to provide toxicological and environmental information resources. The Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA), and its successor legislation, the Superfund Amendments and Reauthorization Act (SARA) of 1986, are cases in point. Although the NLM is not specifically identified in these laws, many of NLM's current activities in toxicology information are now supported under this comprehensive legislation through interagency agreements with Congressionally mandated lead agencies, especially EPA and ATSDR. A graphic representation of the TIP budget over the years is shown in Figure 5.

TIP operates under the authority of the National Library of Medicine Act of 1956 (P.L. 84-941). This Act provides sufficient general legal authority, but does not specifically recognize NLM's activities in the acquisition, organization, and dissemination of information about toxicology and health effects of the

environment. It may be desirable for the NLM Act to acknowledge NLM's roles in these areas.

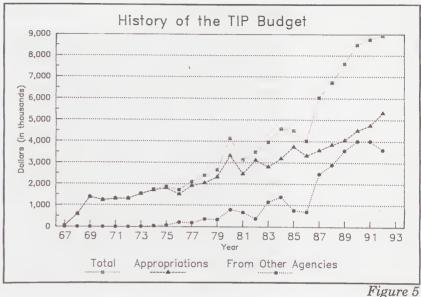
Recommendation 3.3

NLM's authority should be amended to enunciate specifically the Library's continuing and expanding responsibilities in the areas of toxicology and environmental health.

3.4 Obtain Expert Advice on Long Range **Management Principles** for the Toxicology **Information Program**

In 1969, NLM began what was to become a long-lasting relationship with the National Academy of Sciences with the establishment of an advisory committeethe Toxicology Information Program Committee (TIPCOM). Over the years, TIPCOM's membership of illustrious toxicologists, pharmacologists, and chemists, has guided the program. NLM continues to need policy guidance as well as assistance in identifying emerging areas in toxicology and environmental health that may require information support. NLM also needs detailed operational and technical guidance on selecting databases and applying new information technologies.

As described earlier, NLM needs assistance from a users' group to obtain feedback on the technical performance, usability, and acceptability of current database offerings and those under development. If organized under the auspices of TIPCOM—perhaps as a subcommittee—such a group could function as a channel through which



both the TIPCOM membership and NLM management are routinely informed of the user community's needs and expectations. To carry out this expanded charge the current TIPCOM membership would need to be expanded to include representatives of related disciplines (e.g., occupational health, environmental health, computer sciences, database management, and user-system interface development).

Recommendation 3.4

The National Academy of Sciences Toxicology Information Program Committee (TIPCOM) should be expanded in membership and scope of responsibility, and assume a more vigorous role in advising NLM in operational and technical matters, program policy, and new areas of science that should be addressed. A user advisory group comprised of representatives of NLM's enhanced user community should be organized under the auspices of TIPCOM to provide needed feedback on current and anticipated database offerings.

Appendix A History of the Toxicology Information Program of the National Library of Medicine

Background

The 1960s were an era of growing public environmental awareness. The publication in 1962 of Rachel Carson's *Silent Spring* (1) was a powerful spur to the American public and the Congress to take action to protect the environment. A 1966 report by the President's Science Advisory Committee (PSAC) outlined issues related to the effects of hazardous chemicals on the environment and human health. The report not only presented an early discussion on the significance of toxicology to society, it highlighted the importance of ready access to information.

The report suggested that the Department of Health, Education, and Welfare (now the Department of Health and Human Services) was the appropriate agency to develop an information program in this area. President Johnson accepted the recommendations of this report and, as a result, the Department directed the National Library of Medicine to establish a Toxicology Information Program.

At the start, Dr. Martin M. Cummings, then NLM Director, had anticipated receiving approximately 40 personnel positions with an annual budget of several million dollars for the Program. But after a few years it became apparent that TIP would be limited to less than half the positions and to about a million dollars annually. The plans had to be restricted and TIP, thereafter, had to proceed on a much smaller scale than had been hoped for.

In 1969, the Program started what was to become a long-lasting relationship with the National Academy of Sciences for the establishment of an advisory committee—the Toxicology Information Program Committee (TIPCOM). It was intended that this group would be a channel through which the information needs and opinions of academic and industrial biomedical scientists could be brought to the attention of the TIP. Furthermore, all projects that the Program has undertaken have been passed in review before this group.

The scope of information covered by NLM's toxicology files has evolved over the years. Originally slanted more toward adverse health effects of selected drugs and chemicals, the files currently are influenced by a much broader and deeper assortment of societal concerns about chemicals and other contaminants. Some of this is mandated by recent environmental legislation, as shown by specific information-related mandates in such major laws as the Toxic Substances Control Act of 1976 and the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (the "Superfund" legislation) and its amended version of 1986.

Such mandates for new, environmentally related information activities and services had major impacts on the scope and nature of NLM's service. In many instances, the agency charged in the legislation with implementation of such activities started to collaborate with NLM and built the new activities by enhancing existing NLM services. For example, ATSDR now provides substantial support to NLM for the maintenance of the Hazardous Substances Data Bank (HSDB) which furnishes detailed information on the properties, emergency handling, environmental fate and regulatory requirements for over 4,200 hazardous chemicals.

The substantial contribution of funding from other agencies in support of projects of mutual interest has been helpful. In fact, certain projects could not have been started or sustained without such support. However, there is a downside to obtaining basic funding support for projects from others, because it ties the fate of the supported projects to the fortunes of the other agency. It would be preferable if funds for such collaborative projects could be shifted to NLM at the Congressional appropriations level and thus become part of the NLM budget.

Information Services

Reference Services

From its inception, TIP has provided references services in response to queries from the biomedical community. However, because internal staff resources were insufficient for a full-fledged service, an interagency agreement with the Atomic Energy Commission (now the Department of Energy) was established and used to set up in 1972 a Toxicology Information Response Center (TIRC) at the Oak Ridge National Laboratory (ORNL). TIRC searched NLM databases and other sources, and furnished comprehensive literature searches to requestors on a fee-for-service basis.

Over the years, the increasing availability and popularity of online retrieval services in toxicology has greatly diminished the demand for the kind of specialized reference service provided by TIRC in the 70s. The Center is still in operation but its size has been reduced; it now provides responses to some 15 search requests per month, and many of these come from the ORNL science community itself.

Publications

While the main method by which the TIP now provides information to its clients is via its online computer services, initially the Program put a certain amount of effort into publishing bibliographies. monographs and periodicals. Among the titles published over the years (some in collaboration with other organizations) were: Drug Interactions: An Annotated Bibliography with Selected Excerpts (1967-1971); Toxicity Bibliography (1968-78); A Directory of Information Resources in the United States: General Toxicology (1969); Pesticides Abstracts: Abstracts on Health Effects on Environmental Pollutants; Toxicology Research Projects Directory; Tox-Tips (Toxicology Testing in Progress) (1976-87); Symposium on the Handling of Toxicological Information (1976); NTP Chemical Registry Handbook (1981); Proceedings of the Symposium on Information Transfer in Toxicology (1982); Alternatives to the Use of Live Vertebrates in Biomedical Research and Testing: An Annotated Bibliography (1988).

Online Bibliographic Services

TOXLINE, the first online bibliographic system for toxicology, was developed by the TIP in 1972 as a "one-stop shopping center" for toxicology information. The original intent to follow the MEDLINE lead and "mechanize" an existing abstracting and indexing (A&I) source for online bibliographic retrieval had to be adjusted because no one secondary source covered the field of toxicology sufficiently. It was decided, therefore, to combine "toxicology subsets" from various A&I services into one file that would look reasonably homogeneous to the online user. Thus, TOXLINE initially incorporated relevant segments from

Index Medicus, Biological Abstracts, Chemical Abstracts, and International Pharmaceutical Abstracts. Over the years other segments have been added while some had to be deleted. TOXLINE also served to validate the utility of whole-text searching without a controlled vocabulary. This was accomplished by creating one large inverted file of all searchable terms.

Several of the TOXLINE segments were obtained from A&I services under usage royalty agreements. The costs were passed on to the users and, over time, increased to where TOXLINE became substantially more expensive than other NLM online services. License arrangements, not involving usage royalties, could be developed for some segments. notably those from Biological Abstracts and International Pharmaceutical Abstracts. However this did not prove feasible with Chemical Abstracts. In 1987, it was decided to split TOXLINE into a new usage royalty service called TOXLIT (and its backfile TOXLIT65), which contained the Chemical Abstractsderived segments, and another service, without such royalties, for which the name of TOXLINE was kept. This family of services now contains more than 3 million records.

Online Chemical Dictionaries and Directories

Because toxicology is concerned with the effects of chemicals on biological systems, the accurate identification of chemical substances is often a critical preliminary to utilizing toxicology information systems. For TOXLINE, this problem was met by building CHEM-LINE, an online chemical dictionary file that derived its content mainly from the Chemical Abstracts Service (CAS) Registry System. CHEMLINE was the forerunner of the class of online chemical information directories in that it linked nomenclature, structural information and CAS Registry Numbers to the location of information about a specific chemical or groups of structurally related chemicals in other files. CHEMLINE made two fundamental contributions to chemical information retrieval: it demonstrated the importance of the CAS Registry Number in online information seeking, and it showed that fragments derived from parsing standardized chemical nomenclature could provide useful online substructure searching capabilities.

Over the years, as more NLM files with chemical subject content became available, CHEMLINE expanded its directory function by pointing users to these other NLM files where information about a chemical or a family of chemicals might be found. To obtain the data needed to build CHEMLINE, an agreement involving usage royalties was reached with CAS. It gave NLM access to certain computer-produced portions of the CAS Registry System. As was the case for TOXLINE, NLM adopted a policy whereby the royalty charges arising from the use of CAS information were passed on to the users of CHEMLINE. Because CAS has steadily raised those royalty charges, TIP developed a new, royaltyfree chemical information resource named ChemID (Chemical IDentification) that now contains some 200,000 records. ChemID was created using a variety of royalty-free sources. It still functions as a chemical dictionary with nomenclature, synonyms, and CAS Registry Numbers, and as a directory with pointers to the location of information about chemicals in other MEDLARS

files, with the exception of the royalty-based TOXLIT and TOXLIT65 files. ChemID was made available to the public in February 1990.

In July 1990, ChemID's directory functions were substantially expanded with a new set of data collectively known as SUPERLIST. This capability provides the names and other chemical identifiers used on a variety of regulatory or scientific lists. With the proliferation of Federal, state, and international lists of chemicals, the presence of a chemical on such a list can have important regulatory or financial consequences for government agencies as well as for commercial organizations. At the present time, this coverage includes 20 lists such as the Department of Transportation Hazardous Materials List, EPA Pesticide List, OSHA Toxic and Hazardous Substances, and the IARC (International Agency for Research on Cancer) list.

Online Data Banks

Bibliographic retrieval systems—online or hard copy—are fact locators in that they direct the user to journal articles or books that contain the sought-for facts. In contrast, data or fact retrieval systems—like handbooks—provide users with the actual facts.

Having organized TOXLINE, the bibliographic retrieval service for toxicology, the Toxicology Information Program turned, in 1974, to the creation of the Toxicology Data Bank (TDB), an online-searchable compilation of referenced numeric data and textual statements about the chemical and biological properties of some 3000 drugs and hazardous chemicals. Data statements were extracted from published sources such as

textbooks, monographs, Government reports and, to a lesser extent, journal articles. The file was organized by compound, and records were reviewed periodically for validity and accuracy by a special review group—the Scientific Review Panel (SRP). The "grant-like" review process of reviewing TDB records is a unique way of reviewing the content of scientific documents by a committee. The TDB was later renamed the Hazardous Substances Data Bank (HSDB).

TOXNET

Initially, the TDB was maintained and provided to the public through ELHILL, NLM's major file building and information retrieval system. However, that system was originally designed for efficient bibliographic retrieval from large files with many, relatively small records. It never functioned well for the kind of data retrieval required for the TDB. When it became clear that ELHILL would not be able to handle the large data records resulting from the expansion of the TDB to the HSDB, the Program developed a new system, named TOXNET.

TOXNET is a multicomponent system that allows for online file building, content review and revisions, as well as online, interactive searching. Access to TOXNET is available to all NLM users. Through a gateway that links the TOXNET computers to the NLM mainframe, TOXNET users also can readily access relevant NLM bibliographic files such as MEDLINE or TOXLINE. Online usage of the TOXNET files continues to grow and now averages 1600 hours per month; another 250 hours are used for gateway access to the files on the NLM mainframe.

The following files (and their sponsoring organizations) are available on TOXNET:

Chemical Carcinogenesis Research Information System (CCRIS), NCI

Developmental and Reproductive Toxicology (DART), EPA & NIEHS

Environmental Mutagen Information Center (EMIC), EPA & NIEHS.

 $EMICBACK\ (Backfile\ for\ EMIC)$

ETICBACK (Backfile for DART)

Genetic Toxicology (GENETOX), EPA.

Hazardous Substances Data Bank (HSDB), NLM & ATSDR

Integrated Risk Information System (IRIS), EPA

Registry of Toxic Effects of Chemical Substances (RTECS), NIOSH

Toxic Chemical Release Inventory for 1987, 1988, 1989, 1990, EPA

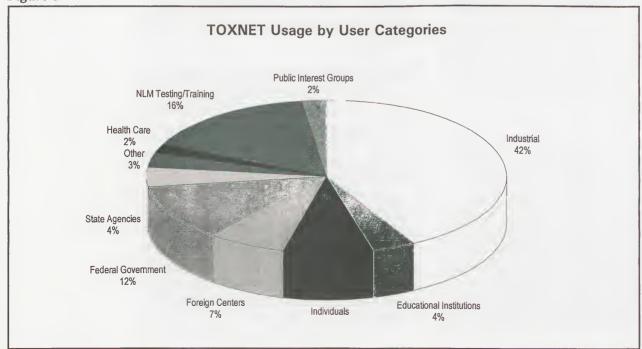
While most TOXNET files take their content from published scientific

sources, one family of files—EPA's Toxic Chemical Release Inventory (TRI)—contains data on chemical releases reported by industry to the EPA as mandated by the SARA legislation. This set of files includes substantial amounts of numeric data, and for it, TOXNET had to be enhanced with statistical, ranging, sorting and menu-based searching capabilities.

Users

When a user organization applies for an access code to the NLM online services, its affiliation is recorded (e.g., industrial, Federal government, state government). Usage is then tracked for billing purposes, and it is relatively easy to link usage by file to user classes. Applying some recent use figures for the files on the TOXNET system as indicative of the usage of the Library's toxicology files in general shows the distribution diagrammed in Figure 6.





Because the Library does not normally examine the computer interactions involved in a user's search session, it is more difficult to obtain reliable data concerning the purposes for which the NLM online services are being used. In order to gather some information about what users are expecting to garner from the toxicology data files on TOXNET, a preliminary user needs assessment was carried out in July 1991. Toxicity and health effects led the list of types of information sought by those responding to the survey. A large number of respondents also indicated a need for the types of information found in the TRI (Toxic Chemical Release Inventory) files.

Systems Redesign

As TOXNET grew in size and usage, it became clear that NLM needed to consider some fundamental changes in the basic design of the system. Because the TOXNET MIIS language/operating system functioned primarily on Data General minicomputers, TOXNET was tied to use of this equipment. Equipment costs were high and future support for this line of hardware was cloudy.

An evaluation study of TOXNET, carried out in 1989 by a team of outside computer scientists, recommended that NLM rewrite the system in a variant of the MUMPS language, which is available to operate on many hardware platforms. This recommendation was followed, and TOXNET now operates in standard ANSI MUMPS on a cluster of microcomputers. This state-of-the-art configuration is more efficient and less costly than the previous system.

In parallel with this effort, it was also decided to explore the use of Relational Database Management System (RDBMS) technology for the family of files now on TOXNET. True file integration would result in more efficient file management, and allow various approaches to the data supporting a variety of user purposes. Conceptually, TOXNET lends itself well to such an approach because it contains multiple files with related—sometimes duplicative—information.

In June 1991, NLM convened a panel of computer experts to address the question of whether relational technology is suitable for these databases. This panel recommended that NLM proceed with developing an RDBMS-based file building module for the HSDB and some of the other TOXNET files but, for the time being, stay away from converting the entire TOXNET system to a relational system, because none of the existing RDBMS packages are efficient enough in online searching of highly textual files such as many of those on TOXNET.

Emergency Response

The Superfund Act included requirements for support of emergency response activities in cases of accidents involving hazardous chemicals. In response to these mandates, ATSDR collaborated with NLM, to build a transportable, microcomputer-based workstation that provides information assistance to emergency response teams working on such accidents. The operational prototype, known as ANSWER (an acronym for ATSDR-NLM's Workstation for

Emergency Response), consists of software modules designed to facilitate easy access to information useful to response teams during emergencies.

The core modules of the Workstation are: a CD-ROM containing databases with information on both hazard management and medical management; a special database with information gleaned from previous chemical emergencies; a modified version of software (Micro-CSIN) that facilitates searching of diverse, remote online databases; a FAX capability to transmit information to and from an emergency site; access to weather information from the National Weather Service; and a word processing capability for dealing with retrieved data.

The Workstation was made available for Beta testing at 13 sites, including selected state health departments and several poison control centers. The results of the test showed that ANSWER is highly useful in a command center environment in both emergency and nonemergency situations, and that additional chemical databases on CD-ROM would be very helpful in the field.

Issues

Several issues of potential significance for the future of the Toxicology Information Program can be extracted from its 24-year history:

When taking inflation into account, the NLM portion of the TIP budget has remained constant since 1968. However, several new products were developed with funds from collaborating agencies and with funds collected from users. Funding through other agencies is

intrinsically unstable because it depends on their budgets and program objectives.

Leasing files from organizations that require usage royalties was useful because it brought valuable content to the NLM files. However, the steady increase in these royalties made it necessary to restructure the NLM files into royalty and nonroyalty services so that users that could not afford the higher charges, could still make use of a portion of the information.

In part, NLM evaluates the utility of its online files by the amount of usage. In recent years, several of these files have been leased from NLM by the vendors of CD-ROM products for incorporation in commercial CD-ROM products. As these products become more widely accepted, usage of NLM's online files will decrease without NLM being able to measure the offsetting uses of the commercial CD-ROM products.

Generally, NLM services are intended for use by scientists and health professionals. However, the Toxic Chemical Release Inventory (TRI) files on TOX-NET are clearly meant by law to be available and accessible to the general population. This altered focus placed new requirements for ease of access and simplicity of content on the Program.

Searching NLM's online toxicology files is difficult. This has put a substantial training burden on the Program. In the future, such training costs should be included when considering the cost-effectiveness of online systems. In the long run, a more expensive, easy-to-use system may be cheaper than a complex system requiring training courses and teaching packages.

Conclusion

The 25 years since issuance of the PSAC report have seen a steadily increasing concern, worldwide, with the threats to human welfare stemming from environmental contamination. Widely available, reliable scientific and technical information is an important tool in the campaign to clean up the environment and protect human health. The Toxicology Information Program has been an active participant in this campaign for a quarter century and is ready to embrace a continuing and expanded role in the future.

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Appendix B Glossary

A&I Services	Abstracting and Indexing Services, also called secondary publication services
ANSI	American National Standards Institute, an organization that develops and publishes industry standards. A source of standards for computers and communications technologies.
ANSWER	. ATSDR/NLM Workstation for Emergency Response
ATSDR	Agency for Toxic Substances and Disease Registry, the Superfund agency in the Public Health Service
Beta Test	. Individuals or organizations used for final testing/acceptance
BIOSIS	Biological Information Service, a product of Biological Abstracts, the major U.S. A&I service for biology
CAMEO	Computer Aided Management of Emergency Operation, software designed by the National Oceanic and Atmospheric Administration.
CANCERLIT	. CANCER LITerature, a bibliographic file on ELHILL
CAS	. Chemical Abstracts Service, a division of the American Chemical Society. CAS is the world's major A&I service for chemistry.
CAS Registry System	A CAS-developed and operated computer system that stores structure and nomenclature information for ca. 11 million chemical substances and assigns unique numbers (the CAS Registry Numbers) to the records of these substances.
CCRIS	. Chemical Carcinogenesis Research Information System, an NCI database on TOXNET
CDC	. Centers for Disease Control and Prevention
CD-ROM	. Compact Disk-Read Only Memory
CERCLA	Comprehensive Environmental Response, Compensa- tion and Liability Act of 1980, also known as the Superfund Act
ChemID	. Chemical IDentification, a non-royalty chemical nomen- clature and directory file on ELHILL
CHEMLINE	. CHEMical Dictionary ONLINE, a royalty chemical nomenclature and directory file on ELHILL
COACH	Expert search system prototype used to improve retrieval from MEDLINE with Grateful Med
Crossfile Searching	

CSIN	Chemical Substances Information Network, a hardware software facility, developed in the mid-70s, to search databases with chemical substances information located on various computer systems; cf. Micro-CSIN
DART	Developmental and Reproductive Toxicology, a bibliographic file on TOXNET
DBMS	Database Management System, a class of software used to build and maintain computer databases
DHHS	Department of Health and Human Services, component of the U.S. Government
DIRLINE	DIRectory of Information Resources OnLINE, a directory database on ELHILL
Distributed Network	An arrangement of computers on a network which work together in a cooperative manner
EC	European Community
EIS	Emergency Information System, a service provided by Research Alternatives Inc. of Rockville, MD
ELHILL	MEDLARS software named after Senator Lister Hill
EMIC and EMICBACK	Environmental Mutagen Information Center database (and its backfile), a bibliographic file on the TOXNET system, sponsored by EPA and NIEHS and produced by the Oak Ridge National Laboratory
EPA	Environmental Protection Agency, an agency of the U.S. Government
ETIC and ETICBACK	Environmental Teratology Information Center database (and its backfile). ETIC has been replaced by DART (see). ETICBACK is a bibliographic file on TOXNET; it was sponsored by EPA and NIEHS
	A computer program that combines knowledge of a particular subject with inferencing mechanisms that enable it to use this knowledge in problem-solving situations
	Food and Drug Administration, an agency of the Public Health Service
	Federal Coordinating Committee for Science, Engineering and Technology, a White House-based facility established to coordinate designated scientific and technical matters across the Federal Government
	Literature appearing outside of traditional publication channels (e.g., technical reports, government documents, corporate memoranda, etc.)

Gateway	A mechanism providing access among multiple systems and databases
Good Laboratory Practices	Laws and regulations covering all phases of toxicology testing
GenBANK	A DNA sequence database now operated by NLM's National Center for Biotechnology Information
GENE-TOX	GENEtic TOXicology, an EPA-sponsored database on TOXNET
Grateful Med	An NLM-developed software package for IBM and Macintosh microcomputers that facilitates searching of MEDLINE and other NLM online files
HSDB	Hazardous Substances Data Bank, an NLM-maintained file on the TOXNET system that describes the chemical, biological and environmental properties of some 4300 chemicals
HAZMAT	HAZardous MATerials; term often used in connection with activities related to the response to and prevention of chemical accidents
HBCUs	Historically Black Colleges and Universities
HPCC	High Performance Computing and Communication, a current Presidential initiative area
IARC	International Agency for Research on Cancer, an NCI- supported facility in Lyons, France
ILO	International Labour Organization, a U.N. organization
IM	Index Medicus, an NLM publication
Informatics	See Medical Informatics
Information Sources Map	A component of the UMLS (see) containing information about the scope, location, vocabulary, syntax rules, and access conditions of biomedical databases of all kinds
	International Program for Chemical Safety, a U.N. program
IRIS	Integrated Risk Information System, an EPA-produced database on TOXNET
	International Registry for Potentially Toxic Chemicals, a U.N. organization
ISM	See Information Sources Map

Matarial Cafeta	
Material Safety Data Sheet	Informational materials describing properties including hazards to human health, and protective measures connected with chemical substances in commerce; established by the Hazard Communication Standard and regulated by OSHA (see)
Medical Informatics	The study of medical information, including medical decision-making, cognitive processes, human-machine interface, knowledge representation, and information storage and retrieval.
MEDLARS	MEDical Literature Analysis and Retrieval System, NLM's network of online services
MEDLINE	MEDical Literature OnLINE, NLM's major bibliographic file on ELHILL
MeSH	Medical Subject Headings, NLM's indexing thesaurus
Metathesaurus	A component of the UMLS (see) containing information about biomedical concepts and their representation in different vocabularies and thesauri
Micro-CSIN	Microcomputer-based version of CSIN (see), developed for information gathering to support responses to chemical emergencies
MIIS	Meditech Interpretative Information System, a dialect of MUMPS (see)
MSDS	Material Safety Data Sheet (see)
MUMPS	Massachusetts General Hospital Utility & Multi-Programming System, the programming language used for TOXNET
NAS	National Academy of Sciences
	Directory database on DIRLINE, formerly produced by the Library of Congress
NCI	National Cancer Institute, an NIH institute
NIEHS	National Institute of Environmental Health Sciences, an NIH institute
	National Institutes of Health, an agency of the Public Health Service
	National Institute for Occupational Safety and Health, a CDC organization
NLM	National Library of Medicine, an NIH institute

NN/LM	. National Network of Libraries of Medicine, coordinated by NLM, includes over 3,600 U.S. health science libraries
NRC	. National Referral Center (see)
NREN	. National Research and Education Network
NTP	. National Toxicology Program, an inter-agency program administered by NIEHS (see)
OECD	Organization for Economic Cooperation and Development, an international organization that includes representation from the major industrialized countries
ORAU	Oak Ridge Associated Universities, a multi-university organizational structure maintained by the Department of Energy
ORNL	Oak Ridge National Laboratory, one of the national R&D organizations supported by the Department of Energy
OSHA	Occupational Safety and Health Administration, an agency in the Department of Labor concerned with the safety and health of workers
PHS	. Public Health Service (see)
PSAC	President's Science Advisory Committee, a multi-disci- plinary organization that functioned during the 60s and 70s to provide advice on science matters to the President
Public Health Service	. A multi-agency (viz., CDC, FDA, NIH) organizational component of the Department of Health and Human Services
RFA	. Request for Application (for grant applications)
Risk Assessment	. In the health area, the use of available information to evaluate and estimate exposure to a hazardous agent and its consequent adverse health effects
RTECS	Registry of Toxic Effects of Chemical Substances, a NIOSH produced database provided online through the TOXNET system
RML	Regional Medical Library, major health science libraries in eight regions of the U.S. that are under contract to NLM to support various NLM activities such as interlibrary loans and training
SARA	. Superfund Amendments and Reauthorization Act of 1986
SIS	Specialized Information Services, the NLM Division that manages the Toxicology Information Program

SRP	Scientific Review Panel, the group of experts in toxicology, medicine and the environmental sciences that regularly reviews the content of the HSDB (see)
Superfund	See CERCLA
SUPERLIST	A capability built into ChemID (see) that permits users to identify important regulatory and scientific lists pertaining to a particular chemical
TDB	. Toxicology Data Bank, NLM's original online databank describing the properties of hazardous chemicals. Now superseded by HSDB (see)
TIP	. Toxicology Information Program, a program established at NLM in 1967
TIPCOM	. Toxicology Information Program COMmittee, a National Academy of Sciences advisory committee for the Toxicol- ogy Information Program
TIRC	Toxicology Information Response Center, an NLM- supported facility at the Oak Ridge National Laboratory that provides information and performs literature searches for clients in toxicology and related areas
TOMES	Toxicology, Occupational Medicine, and Environmental Series, a CD-ROM database with medical treatment information for chemical exposure emergencies, produced by Micromedex, Inc.
Toxic Chemical	
Release Inventory	An EPA activity mandated under the "Emergency Planning and Right to Know" section of the 1986 Superfund Amendments and Reauthorization Act. (cf.TRI)
TOXLINE	TOXicology Information OnLINE, a multi-component, non-royalty bibliographic file on ELHILL, covering the subject area of toxicology broadly
TOXLINE65	TOXLINE backfile
TOXLIT	TOXicology LITerature, a royalty-based bibliographic file on ELHILL, similar to TOXLINE, but composed entirely of material provided by Chemical Abstracts Service (see)
TOXLIT65	TOXLIT backfile
	TOXicology Data NETwork, NLM's microprocessor- based system for building, maintaining and online delivery of databanks in toxicology and related areas

TRI	Toxic Chemical Release Inventory (see), a series of files created by EPA from industry submissions on annual environmental releases. Available online on the TOXNET system
TSCA	Toxic Substances Control Act, legislation passed in 1976 that controls (inter alia) the distribution of newly developed industrial chemicals and new uses of existing chemicals
UMLS	Unified Medical Language System, an NLM project to create linkages among major thesauri used to index medical information
UNEP	United Nations Environment Programme, a component organization of the U.N.
WHO	World Health Organization, a component organization of the U.N.

Appendix C Footnotes

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U.S. Department of Health and Human Services
Public Health Service
National Institutes of Health

Publication No. 94-3486